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PATENT

GROUP 1800

Attorney Docket No. 11823-002630

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Cary L. Queen et al.

Serial No.: 08/484,537

Filed: June 7, 1995

For: IMPROVED HUMANIZED  
IMMUNOGLOBULINS

Examiner: Julie Reeves

Art Unit: 1806

PRELIMINARY AMENDMENTCommissioner of Patents and Trademarks  
Washington, D.C. 20231**OFFICIAL**

Sir:

In addition to the preliminary amendment in the present application dated June 7, 1995, please amend as follows:

IN THE CLAIMS:

Please add the following new claims:

--106. A method of producing a humanized immunoglobulin against a preselected antigen, said method comprising the steps of expressing, in a host cell, first and second polynucleotides respectively encoding heavy and light chains of a humanized immunoglobulin having complementarity determining regions (CDRs) from a donor immunoglobulin and heavy and light chain variable region frameworks from human acceptor immunoglobulin heavy and light chains, which humanized immunoglobulin specifically binds to the antigen with an affinity constant stronger than  $10^7 M^{-1}$ , wherein said humanized immunoglobulin heavy chain comprises one or more amino acids from the donor immunoglobulin heavy chain framework outside the Kabat and Chothia CDRs, wherein the donor amino acids substitute for corresponding amino acids in the acceptor immunoglobulin heavy chain framework, and each of these said donor amino acids contains an atom within a distance of 6 Å of a CDR in said humanized immunoglobulin; and